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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/667,625 | 09/22/2003 | Nalini M. Rajamannan | 07039-163003 | 1186 |

26191 7590 11/03/2004

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| EXAMINER | |
|---|---|
| NGUYEN, QUANG | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/667,625 | RAJAMANNAN, NALINI M. | |
| | Examiner | Art Unit | |
| | Quang Nguyen, Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 34-35 are pending in the present application, and they are examined on the merits herein.

### *Specification*

Please update the current status of US application serial no. 09/399,704, filed September 21, 1999, now US Patent 6,660,260 in the first paragraph of the specification.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Choy et al. (Developmental Dynamics 206:193-200, 1996) as evidenced by Dunstan et al. (US 5,656,598).

Claim 34 is drawn to a method for identifying an inhibitor of heart valve degeneration, said method comprising: a) contacting heart valve cells with a stimulant such that said cells proliferate, b) contacting said cells with a test compound, and c) determining if said test compound reduced the proliferation of said cells, wherein the reduction of proliferation indicates that said test compound is an inhibitor of heart valve

degeneration. Claim 35 is directed to a method for determining the safety of a drug, said method comprising: a) contacting heart valve cells with said drug, and b) determining if said drug induced proliferation of said cells, wherein the induction of proliferation indicates that said drug promotes heart valve degeneration.

Choy et al teach a method in which chick atrioventricular valve mesenchymal cells were cultured in the form of three-dimensional aggregates that were exposed to FGF-2. It was determined that FGF-2 stimulated the chick heart valve mesenchymal cell proliferation (see abstract and Fig. 1). Choy et al also teach a method in which the chick heart valve mesenchymal cells were exposed to FGF-2 in the presence of either the peptide Gly-Arg-Gly-Asp-Ser-Pro (GRGDSP) or the control peptide Gly-Arg-Gly-Glu-Ser-Pro (GRGESP) to test the effects of the GRGDSP peptide on the proliferative effects of FGF-2 on the chick heart valve mesenchymal cells (see abstract; page 194, col. 1, last paragraph continues to first paragraph of col. 2). Choy et al reported that blocking the cell surface integrin receptor with GRGDSP inhibited the proliferative response whereas the GRGESP peptide did not effect the FGF-2 response (see Fig. 3). Choy et al further teach that sodium chlorate at 20-100 mM inhibited both the matrigenic and mitogenic responses to FGF-2 by chick heart valve mesenchymal cells (Fig. 4).

With respect to claim 35, FGF-2 is a drug as evidenced by the teachings of Dunstan et al. that disclose therapeutic compositions comprising fibroblast growth factors including FGF-2 for treating patients suffering from pathological conditions in which bone mass is inadequate or in repairing defects in bone or dental tissue (see Summary of the Invention).

Accordingly, the methods taught by Choy et al meet every limitation of the instant claims by having the same steps and materials as recited in the claims. Therefore, the reference anticipates the instant claims.

Claim 35 is rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (J. Mol. Cell Cardiol. 19:1185-1193, 1987; AKKK, IDS) as evidenced by Kunkle, Jr (US 5,955,436).

The claim is directed to a method for determining the safety of a drug, said method comprising: a) contacting heart valve cells with said drug, and b) determining if said drug induced proliferation of said cells, wherein the induction of proliferation indicates that said drug promotes heart valve degeneration.

Johnson et al disclose a method in which porcine cardiac valvular subendothelial cells were cultured in the presence of purified platelet derived growth factor (PDGF), and after 18 hours the cells were pulsed with $^{3}$H-thymidine and assayed to determine the mitotic index (page 1187, section titled "Mitogen assay"). It was determined that purified PDGF stimulates porcine valve subendothelial cells proliferation to a similar extent as it does to cultured smooth muscle cells and skin fibroblasts (see Table 1).

PDGF can be considered as a drug as evidenced by the teachings of Kunkle that show that PDGF is used to enhance wound healing (see abstract).

Accordingly, the methods taught by Johnson et al meet every limitation of the instant claim by having the same steps and materials as recited in the claim. Therefore, the reference anticipates the instant claim.

## *Conclusion*

***No claims are allowed.***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.**

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

*Quang Nguyen, Ph.D.*